OC-0546

Minimally ablative dose (MAD) for the treatment of lung cancer using SBRT: Is it such a "MAD" concept?

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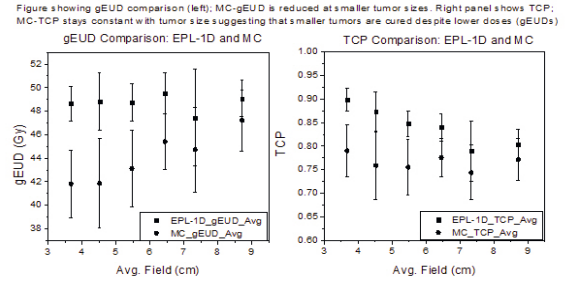
Purpose/Objective: To determine whether individualization of dose prescriptions based on tumor size and location is a feasible approach for SBRT-based treatment of non-small cell lung cancer.

Materials and Methods: Treatment plans for 133 NSCLC patients treated using 12 Gy/Fxn x 4, and planned using a pencil-beam (1D-equivalent-path-length, EPL-1D) algorithm were retrospectively calculated with a Monte Carlo (MC)-based algorithm using EPL-1D plan parameters. 4D imaging was performed to generate an ITV. PTV margin was 5 mm. For each plan, generalized equivalent dose (gEUD) and tumor control probability (TCP with SF=0.28) were computed. Tumors were stratified according to peripheral ('island', N=39), lung-wall (attached to the rib-cage, N=44) and central locations (N=50), as well as tumor size and mean plan field size.

Results: GEUD values for the EPL-1D algorithm were based on prescription doses and ranged from 48-49 Gy for all cases. MC-computed gEUD decreased significantly with decreasing tumor size; values in Gy were 41.9±3.6 for average plan field widths (FW) between 3-5 cm; 43.8±3.2 (5≥FW>7 cm); 45.9±3.3 between (7≥FW>10 cm). TCP's for the EPL-1D algorithm increased with decreasing tumor size with values of 0.88±0.04 (3≥FW>5 cm); 0.85±0.03 (5≥FW>7 cm); 0.80±0.05 (7≥FW>10 cm). On the other hand, MC-computed TCP's remained relatively constant as a function of tumor size; values were 0.77±0.07 (3≥FW>5 cm); 0.76±0.05 (5≥FW>7 cm); 0.76±0.05 (7≥FW>10 cm). Results were consistent for 'island', lung wall and central tumors. There was no correlation between tumor size and local control rate among the 92% of patients who were controlled locally at 2-years, which is consistent with the MC-calculated TCPs. Note, however, that MC-computed gEUDs were significantly lower for smaller tumor sizes. This suggests that although smaller tumors were receiving much lower doses (on average, 10.5 Gy vs. 12 Gy per fxn), they were being controlled. These findings are consistent with radiobiology; smaller tumors have fewer tumor cells and therefore require lower doses to be controlled relative to larger tumors. Results are also suggestive that dose could be tailored according to size and location of the tumor, i.e. one size does not need to fit all. We speculate as well that the concept of minimally ablative dose (MAD) is perhaps not an unreasonable approach to consider for smaller tumors. Dose de-escalation for smaller tumors, based on the mimimum ablative dose is likely to be clinically relevant for tumors situated close to normal organs (e.g. ribs, centrally located airways) and for patients being treated for recurrent disease.

	PTV Volume (cm3)	Avg. Field (cm)	EPL-1D_gEUD (Gy)	EPL-1D_TCP (SF=0.28)	MC_gEUD (Gy)	MC_TCP (SF=0.28)
Lung-island	N=39 27.6 / 29.5	±5.0 / 1.0	±48.7 ± 2.4	0.87 ± 0.04	41.3 ± 3.3	0.74 ± 0.06
Lung-wall	N=44 53.4 / 59.8	±5.9 / 1.5	±49.1 ± 1.7	0.85 ± 0.04	44.7 ± 3.2	0.78 ± 0.05
Lung-central	N=50 45.6 / 41.6	±5.8 / 1.4	±48.6 ± 2.5	0.84 ± 0.05	43.9 ± 3.5	0.77 ± 0.06



Conclusions: Retrospective dose analysis of 133 NSCLC patients treated with SBRT is suggestive that individualization of doses based on tumor size and location may be a feasible approach toward achieving equivalent local control and possibly reducing toxicity based on the clinical circumstances.

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How to identify patient specific rectal sub-region likely responsible of rectal bleeding in prostatic IMRT?

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Purpose/Objective: Current toxicity models in prostate cancer radiotherapy, based on dose-volume histograms, do not enable to identify region in the rectum involved in bleeding. Localize such regions may be crucial in IMRT to decrease rectal toxicity. The goals of this study were:
- firstly to assess the rectal bleeding/local dose correlation using voxel wise statistics on several anatomically different templates (thus avoiding a specific template effect),
- secondly to back propagate the significant regions found on these templates to a specific patient (pts).

Materials and Methods: A total of 93 patients receiving a total dose of 80Gy in the prostate by IMRT were included in the analysis. Rectal bleeding (RB) at two years was analyzed (≥ grade 1). The series was divided in 2 cohorts: one for training (63 pts) and the other one for testing (30 pts). A total of 63 randomly chosen individuals (12/51 with/without RB) 3D CT scans and planned dose were non-rigidly registered towards 10 templates in a 3 step process: one rigid registration and two elastic registrations (demons algorithm). The registrations were designed to ensure accurate alignments of rectums and dose distributions. Dice scores and Dose-Organs Overlap (DOO) were computed on the rectum for each pt on the 10 templates to assess the accuracy of the registration.
Two-sampled t-tests were then performed on each template at a voxel-basis leading to the computation of 3D maps for both, the dose differences (and the p-values) between the mean dose of pts having or not toxicity. Significant regions ($p<0.01$) were then characterized in terms of absolute volume, mean dose difference and localization in the rectum. The last one was defined as the distance of the significant region to the prostate and the seminal vesicles surfaces.
The 10 significant regions from each template were then back propagated, using the same registration method, on 30 'test patients' (6/24 with/without RB) leading to the computation of a probability map of the significant region on the rectum for each test patient. The significant regions for toxicity were then delineated using a majority vote approach.

Results:
Median follow-up was 31 months (6 to 64). Two year RB rate were 20%(95% CI: 12-27).

1. Median Dice and DOO were 0.98 (sd 0.01) and 0.97 (sd 0.02).
2. Significant differences of dose related with toxicity were found in large regions on the 10 templates, corresponding to 5.95% of the rectal volume (in average). The anterior wall of the rectum appears involved in RB on the 10 templates (fig): 92.17% (sd 6.3) of the volume of the significant region were localized within the first 15mm of the rectum close to the prostate. In these regions, pts with RB received 6.7Gy (sd 1.3) more than pts without RB.

Conclusions: The anterior wall of the rectum appears strongly involved in RB. Our templates constitute a library of RB correlated region, which can be used to more precisely identify the region at risk of rectal bleeding for a given patient. This new approach opens the way for patient specific treatment by enabling to add IMRT constraints on region likely responsible of RB.

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Dose/volume-response relations for rectal morbidity using planned and motion-inclusive dose distributions

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